DIFFERENTIAL REGULATION OF GENE EXPRESSION OF PITUITARY INTERMEDIATE LOBE MELANOTROPES AND GLIA FOLLOWING ADJUVANT-INDUCED ARTHRITIS

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ABSTRACT

Adjuvant-induced arthritis (AIA) is commonly used as a model for the effects of chronic pain, especially on the endogenous opioid systems. We studied the effects of AIA on the regulation of the proopiomelanocortin (POMC) system. We examined the gene expression of the two major cell types, the melanotropes and the glia, as well as the immunoreactivity of the afferent dopaminergic innervation of the pituitary intermediate lobe (IL) over the course of three weeks of treatment. The effects were apparent after seven days of treatment, peaked at 14 days and were maintained at these levels after three weeks. Melanotrope POMC mRNA levels decreased significantly; fewer cells expressed POMC mRNA and at a comparatively lower level than in control animals. The post-translationally processed peptide, β-endorphin, was similarly reduced as seen by immunohistochemistry. Dopamine, which acts to tonically inhibit POMC gene expression, was studied using an antiserum to tyrosine hydroxylase (TH), the rate-limiting enzyme in dopamine synthesis; fewer axons containing TH were seen as an effect of AIA. All melanotropes express dopamine D_2 receptors, which protein appears in a short form as well as a long splice variant (D_{2L}). Some melanotropes express considerably more D_{2L} mRNA than others. Following AIA, *in situ* hybridization histochemistry showed a dramatic decline in number of cells expressing D_{2L} mRNA as well as a decrease in the level of D_2 mRNA in the melanotropes still expressing any D_2 receptor mRNA (thus, only the short form may actually be expressed following AIA). The peak of D_2 mRNA decline appeared by seven days of treatment and these levels were maintained throughout the three weeks of treatment. Interspersed among the melanotropes are glial cells; (5-10% of the IL cells). These cells express S-100, a cytosolic calcium-binding protein; a subpopulation co-expresses S-100 and glial fibrillary acidic protein (GFAP), an astrocyte specific intermediate filament protein. The number of cells expressing S-100 decreased in the ventral aspects, while increasing in the dorsal aspects of the lobe. The number of cells expressing GFAP also increased in the dorsal aspects of the lobe as did the number of glia co-expressing S-100 and GFAP. Thus, a sub-population of cells co-expressing S-100 and GFAP was selectively increased by AIA.